PATENT SPECIFICATION

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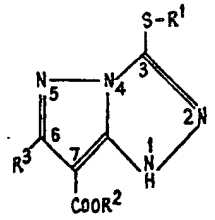
(54) PYRAZOLOTRIAZOLES

(71) We, KODAK LIMITED, a Company registered under the law of England, of Kodak House, Station Road, Hemel Hempstead, Hertfordshire, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention relates to pyrazolo[3,2-*c*-]-*s*-triazoles and to methods of making them.

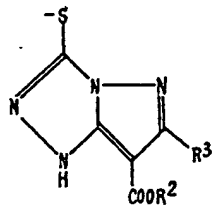
According to the present invention there is provided a compound of the formula:



(I)

wherein

R^1 is hydrogen or an alkyl, substituted alkyl, aryl, substituted aryl or heterocyclic group or a group of the formula:

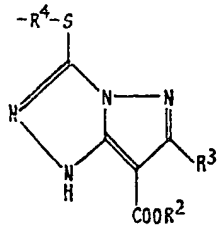


(II)

R^2 is an alkyl group having 1—4 carbon atoms, and

R^3 is hydrogen or an alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic, amino, substituted amino, acylamido, hydroxy, alkoxy or carboxy group or an ester or amide derivative thereof.

Examples of groups which R^1 may represent are straight or branched alkyl groups having 1—22 carbon atoms, carboxymethyl, 1-carboxypent-1-yl, a 2-aminoalkyl, a 2-benzoylaminoalkyl, benzyl, 2,4-dinitrophenyl, 2,4-diaminophenyl or pyridyl group or a group of the formula



(III)

wherein

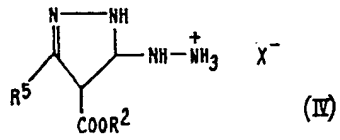
R^2 and R^3 have the meanings given above and

R^4 is an alkylene or alkylarylalkylene group.

Examples of groups which R^3 may represent are straight or branched alkyl groups which may be substituted and preferably contain 1—22 carbon atoms, e.g., methyl, ethyl, n-propyl, isopropyl, sec-butyl, tert-butyl, tert-amyl, tert-pentyl, n-hexyl, n-dodecyl, n-docosyl, 2-chloro-n-butyl, 2-hydroxyethyl, 2-phenyl-ethyl, 2-(2,4,6-trichlorophenyl)ethyl or 2-aminoethyl; aryl radicals which may be substituted, e.g., phenyl, α- or β-naphthyl, 4-methylphenyl, 2,4,6-trichlorophenyl, 3,5-dibromophenyl, 2-, 3- or 4-trifluoromethylphenyl, 2-chloro-α-naphthyl, 3-ethyl-α-naphthyl, 2-methoxyphenyl or a 3-acylamidophenyl; heterocyclic radicals, e.g., pyridyl or thienyl; amino groups; substituted amino groups, e.g., methylamino, diethylamino, n-docosylamino, phenylamino, tolylamino, 4(3-sulphobenzamido)anilino, 4-cyanophenylamino, 2-trifluoromethylphenylamino or benzothiazoloamino; acylamido radicals, e.g., ethylcarbonamido, n-decylcarbonamido, phenylethylcarbonamido, phenylcarbonamido, 2,4,6-trichlorophenylcarbonamido, 4-methylphenylcarbonamido, 2-ethoxyphenylcarbonamido, 2-[(2,4-di-tert-amylphenoxy)acetamido]-benzamido, α- or β-naphthylcarbonamido; a hydroxy group; an alkoxy radical e.g., methoxy, ethoxy, n-butoxy, n-hexoxy, n-dodecyloxy or n-docosoxy; a carboxy or esterified carboxy radical, e.g., methoxycarbonyl, ethoxycarbonyl, n-docosoxycarbonyl or phenoxycarbonyl or a 7-alkoxycarbonylpyrazolo[3,2-*c*]-*s*-triazol-3-yl ethyl group.

The compounds of the present invention are useful intermediates in the preparation of photographic colour couplers and dyes of the cyanine and related types. Because of the presence of the 7-alkoxycarbonyl group this reactive position is protected and it is possible to carry out further chemical reactions, e.g. nitration or oxidation. When required the alkoxycarbonyl group may be simply removed by hydrolysis and decarboxylation by, for example, heating at 180—190°C in orthophosphoric acid under an atmosphere of nitrogen, to provide a 4-equivalent magenta coupler. The 2-equivalent couplers may be prepared therefrom by conventional means.

The compound of formula I may be prepared by the condensation of a pyrazole of the formula:



(IV)

with carbon disulphide in the presence of a base sufficiently strong to liberate the free hydrazine compound, e.g., triethylamine, preferably in the presence of pyridine as solvent. X^- is an anion, R^2 has the meaning given above and R^5 is hydrogen, or an alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic, acylamido, hydroxy, alkoxy, nitro, or carboxy group or an ester or amide derivative thereof. Compounds of formula I wherein R^3 is an amino or substituted amino group may be prepared from appropriate acylamido or nitro compounds by standard methods. This provides the 3-mercapto compound from which the substituted mercapto compounds may be prepared.

The invention is illustrated by the following Examples.

Example 1

Pyridinium 7-ethoxycarbonyl-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-3-thiolate

Ethyl 5-hydrazino-3-methylpyrazole-4-carboxylate hydrochloride (60 g), ethanol (500 ml), triethylamine (37.5 ml) and pyridine (50 ml) were mixed and stirred for 15

minutes. Carbon disulphide (50 ml) was then added, giving a deep brown, clear solution. The mixture was heated on a steam bath, with stirring, for 5 hours and a slow stream of nitrogen was passed through the apparatus to remove hydrogen sulphide. The mixture was allowed to cool overnight, then filtered. The crude product was recrystallised from water (*ca* 400 ml) and dried *in vacuo* at room temperature. A second recrystallisation gave yellow needles (54.9 g, 66%).

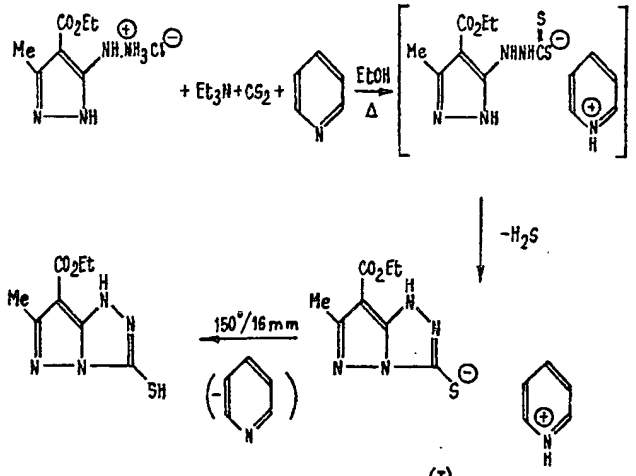
Found:	C 51.00; H 4.95; N 23.00; S 10.40%
$C_{13}H_{15}N_5O_2S$ Requires:	C 51.25; H 4.96; N 22.9; S 10.5%

Ethyl-3-mercapto-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate

A sample of the product was dried at 120—150°/16mm for 2 days, giving the title compound as a buff powder.

Found:	C 42.4; H 4.44; S 14.16%
$C_8H_{10}N_4O_2S$ Requires:	C 42.5; H 4.45; S 14.2%

The reactions employed above are summarised in the following scheme:



(I)

Example 2

Ethyl 6-methyl-3-methylthio-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate

Pyridinium 7-ethoxycarbonyl-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-3-thiolate (7.6 g, 0.025 mole) was suspended in acetone-water (80+50 ml); methyl iodide (3.1 ml, 0.05 mole) in acetone (20 ml) was added. The mixture was stirred for 45 minutes at room temperature, and the resulting solution was partially evaporated *in vacuo*, giving a voluminous precipitate. Water (100 ml) was added, and the solution was chilled and filtered. The dried precipitate (6.17 g) was crystallised from ether-petrol (80/100°) to give colourless needles of ethyl 6-methyl-3-methylthio-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate (5.13 g, 86%) mp 134.5—137°.

Found:	C 45.0; H 4.9; N 23.35; S 12.8%
$C_9H_{12}N_4O_2S$ Requires:	C 45.0; H 5.0; N 22.9; S 13.35%

Example 3

Ethyl 3-n-hexylthio-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate

Pyridinium 7-ethoxycarbonyl-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-3-thiolate (10 g, 0.0328 mole) and n-hexyl iodide (13.8 g, 0.0655 mole) were mixed in acetone (100 ml), and water (20 ml) was added. The mixture was refluxed for 10 minutes and allowed to stand for 1 hour.

The yellow solution so obtained was evaporated to dryness *in vacuo*. The crystalline residue was chromatographed on alumina, eluting with 40/60° petrol, 40/60° petrol: acetone (1:1), and finally acetone. Fractions of *ca* 75 ml were taken.

Evaporation of the eluate *in vacuo* gave a yellow oil, which was crystallised from

40/60° petrol (30 ml). Ethyl 3-n-hexylthio-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate was obtained as colourless crystals (9.11 g, 90%) mp 57.5—61°.

Found:	C 54.05; H 7.11; N 18.13; S 9.98%
$C_{14}H_{22}N_4O_2S$ Requires:	C 54.2; H 7.14; N 18.05; S 10.3%

Example 4

Ethyl 3-n-dodecylthio-6-methyl-1H-pyrazolo[3,2-*c*]-s-triazole-7-carboxylate

Pyridinium 7-ethoxycarbonyl-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-3-thiolate (10 g, 0.0328 mole) was suspended in acetone/water (80+20 ml). Lauryl bromide (15.7 ml, 0.0655 mole) in acetone (20 ml) was added, together with potassium iodide (*ca* 1 g), and the mixture was refluxed for 45 minutes.

The resulting solution was evaporated to dryness *in vacuo*, and the residue was chromatographed on alumina (column 25×1.5 cm; fractions of 75 ml). The column was eluted with petrol (200 ml), petrol/acetone (1:1, 100 ml), and finally acetone (200 ml).

Evaporation of the eluate *in vacuo*, gave an oil, which on scratching, crystallised to a colourless solid. The product was crystallised from petrol (40/60°, 100 ml) as colourless needles (12.0 g, 93%) mp 50—55°. A second recrystallisation from petrol gave ethyl 3-n-dodecylthio-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate as colourless fluffy needles mp 55—56°.

Found:	C 60.9; H 8.6; N 14.3; S 8.0%
$C_{20}H_{34}N_4O_2S$ Requires:	C 60.9; H 8.7; N 14.2; S 8.1%

Example 5

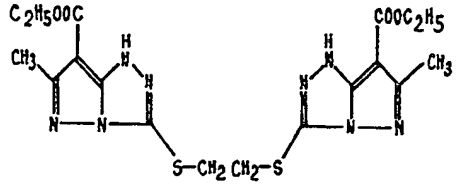
Ethyl 6-methyl-3-2′,4′-dinitrophenylthio-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate

A mixture of ethyl 3-mercapto-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate (2.3 g), 1-chloro-2,4-dinitrobenzene (2.0 g), triethylamine (1.4 ml), acetone (20 ml) and water (5 ml) was heated under reflux for 1 hour during which a yellow solid separated. The mixture was cooled, the solid (2.2 g) was collected and washed with aqueous acetone (50%, 20 ml) and recrystallised from ethanol to give pale yellow crystals of ethyl 6-methyl-3,2′,4′-dinitrophenylthio-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate (1.7 g) mp 280—283°.

Found:	C 42.8; H 3.1; N 21.3; S 8.2%
$C_{14}H_{11}N_6O_8S$ Requires:	C 42.8; H 3.1; N 21.4; S 8.2%

Example 6

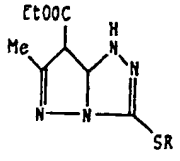
1,4-dithiatetramethylene bis(6-methyl-7-ethoxycarbonyl-1H-pyrazolo[3,2-*c*]-*s*-triazol-3-yl)



A mixture of the pyridine salt of ethyl 3-mercapto-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate (3 g), ethylene dibromide (0.95 g), acetone (25 ml) and water (25 ml) was heated under reflux for 45 minutes. The mixture was then cooled and the ester (1.5 g) was collected. mp. 235—238°.

Found:	C 44.9; H 4.6; N 23.6; S 13.1%
$C_{14}H_{22}N_8O_4S_2$ Requires:	C 45.2; H 4.6; N 23.4; S 13.4%

Further compounds prepared in Examples 7—12 below by methods analogous to the methods employed in Examples 2—5 are of general structure:

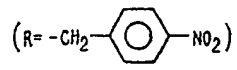


Example 7

$(R=(CH_2)_{17}CH_3)$

Ethyl 6-methyl-3-octadec-1-ylthio-1*H*-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate
m.p. 75—77°

Example 8



Ethyl 6-methyl-3-(4-nitrobenzylthio)-1*H*-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate
m.p. 214—216°.

Example 9

$(R=—CH_2COOH)$

2-(7-Ethoxycarbonyl-6-methyl-1*H*-pyrazolo[3,2-*c*]-*s*-triazol-3-ylthio)acetic Acid
m.p. 246—248° dec.

Example 10

$(R=CH_3(CH_2)\underset{|}{C}HCOOH)$

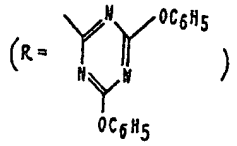
2-(7-Ethoxycarbonyl-6-methyl-1H-pyrazolo[3,2-*c*]-*s*-triazol-3-ylthio)hexanoic Acid
m.p. 179—181°.

Example 11

$(R=CH_2COC_6H_5)$

Ethyl 6-methyl-3-phenacylthio-1*H*-pyrazolo[3,2-*c*]-*s*-triazol-7-carboxylate
m.p. 128—130°.

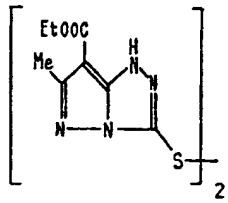
Example 12



Ethyl 6-methyl-3-(4,6-diphenoxy-1,3,5-triazin-2-ylthio)-1*H*-pyrazolo[3,2-*c*]-*s*-trizole-7-carboxylate
m.p. 201—204°.

Example 13

Diethyl 3,3'-dithiodi(6-methyl-1*H*-pyrazolo[3,2-*c*]-*s*-triazole-7-carboxylate)



A solution of iodine (1.25 g) and potassium iodide (5 g) in water (50 ml) was added to pyridinium 7-ethoxycarbonyl-6-methyl-1*H*-pyrazolo[3,2-*c*]-*s*-triazole-3-

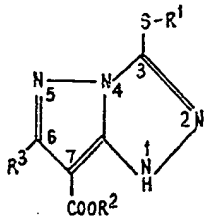
thiolate (3 g) in hot water (70 ml). The precipitate so formed was collected, washed with water and dried in vacuo.

Yield=2.19 g (97%) m.p. 275°.

Found:		C 42.6; H 4.3; N 25.1; S 13.8%
$C_{14}H_{12}N_4O_4S_2$ Requires:		C 42.7; H 4.0; N 24.9 S 14.2%

WHAT WE CLAIM IS:—

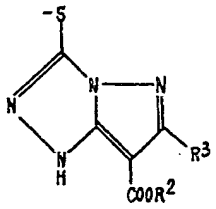
1. A compound of the formula:



(I)

wherein

R^1 is hydrogen or an alkyl, substituted alkyl, aryl, substituted aryl or heterocyclic group or a group of the formula:

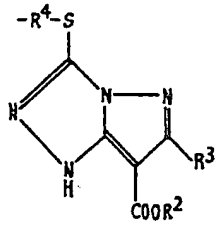


(II)

R^2 is an alkyl group having 1—4 carbon atoms, and

R^3 is hydrogen or an alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic, amino, substituted amino, acylamido, hydroxy, alkoxy or carboxy group or an ester or amide derivative thereof.

2. A compound as claimed in Claim 1 in which R^1 is a group of the formula:



(III)

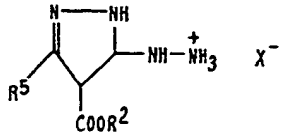
wherein

R^2 and R^3 have the meanings given in Claim 1, and

R^4 is an alkylene or alkylarylalkylene group.

3. A compound according to Claim 1 substantially as described herein and with reference to the Examples.

4. A method of making a compound according to Claim 1 which includes the step of condensing a pyrazole of the formula:



(IV)

with carbon disulphide in the presence of a base sufficiently strong to liberate the free hydrazine compound, wherein

X^- is an anion,
R^2 has the meaning given in claim 1 and
R^3 is hydrogen, or an alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic, acylamido, hydroxy, alkoxy, nitro, or carboxy group or an ester or amide derivative thereof.

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Agent for the Applicants.

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